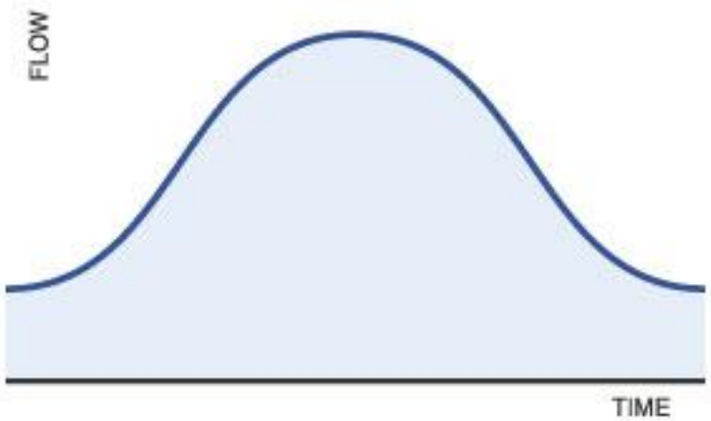
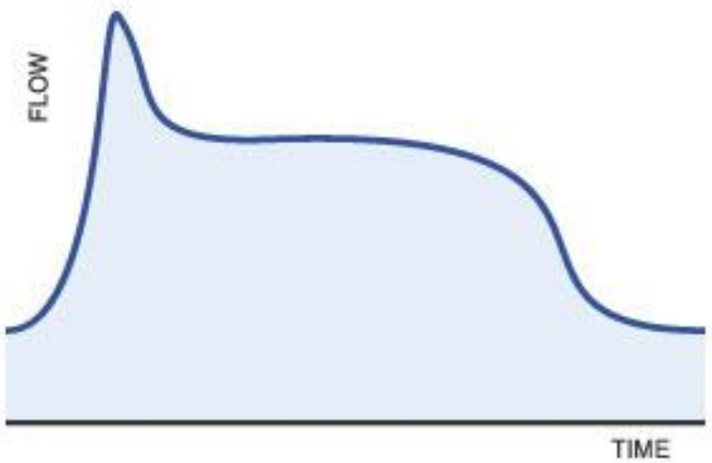
Question

Heart Failure and Sleep Disordered Breathing (SDB) – Unhappy Bedfellows

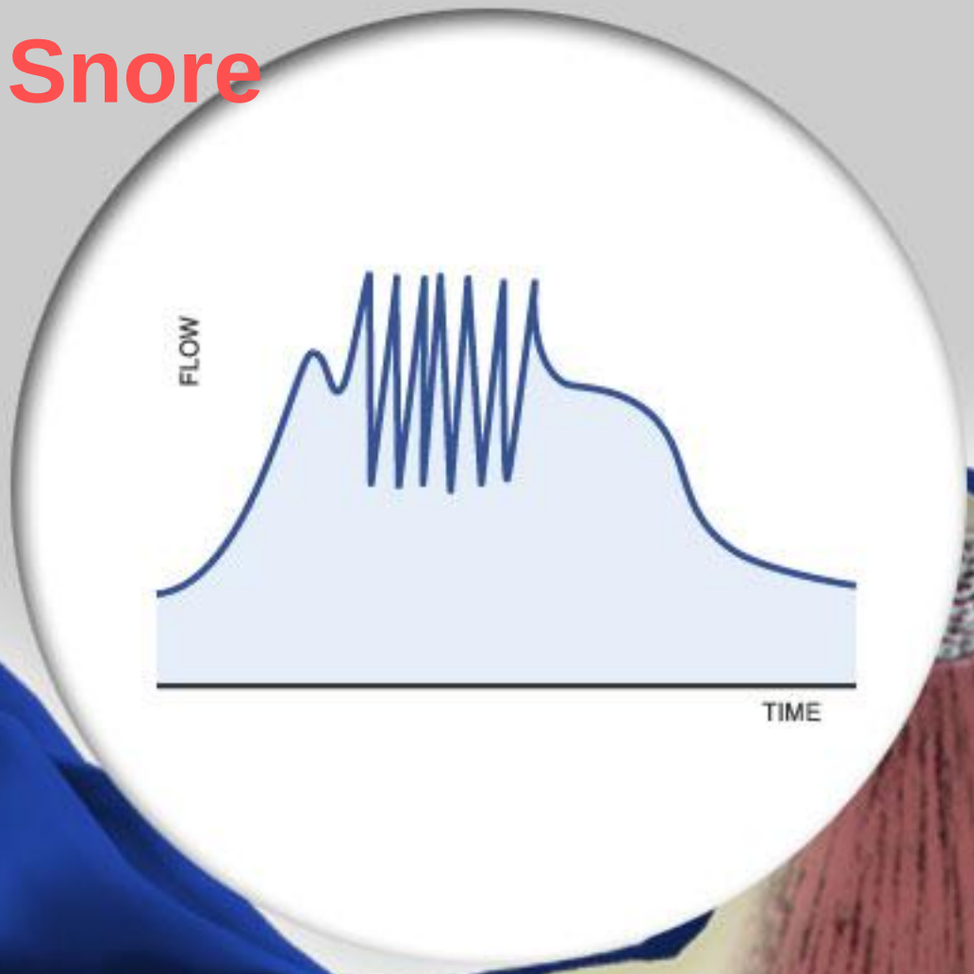
Open Airway



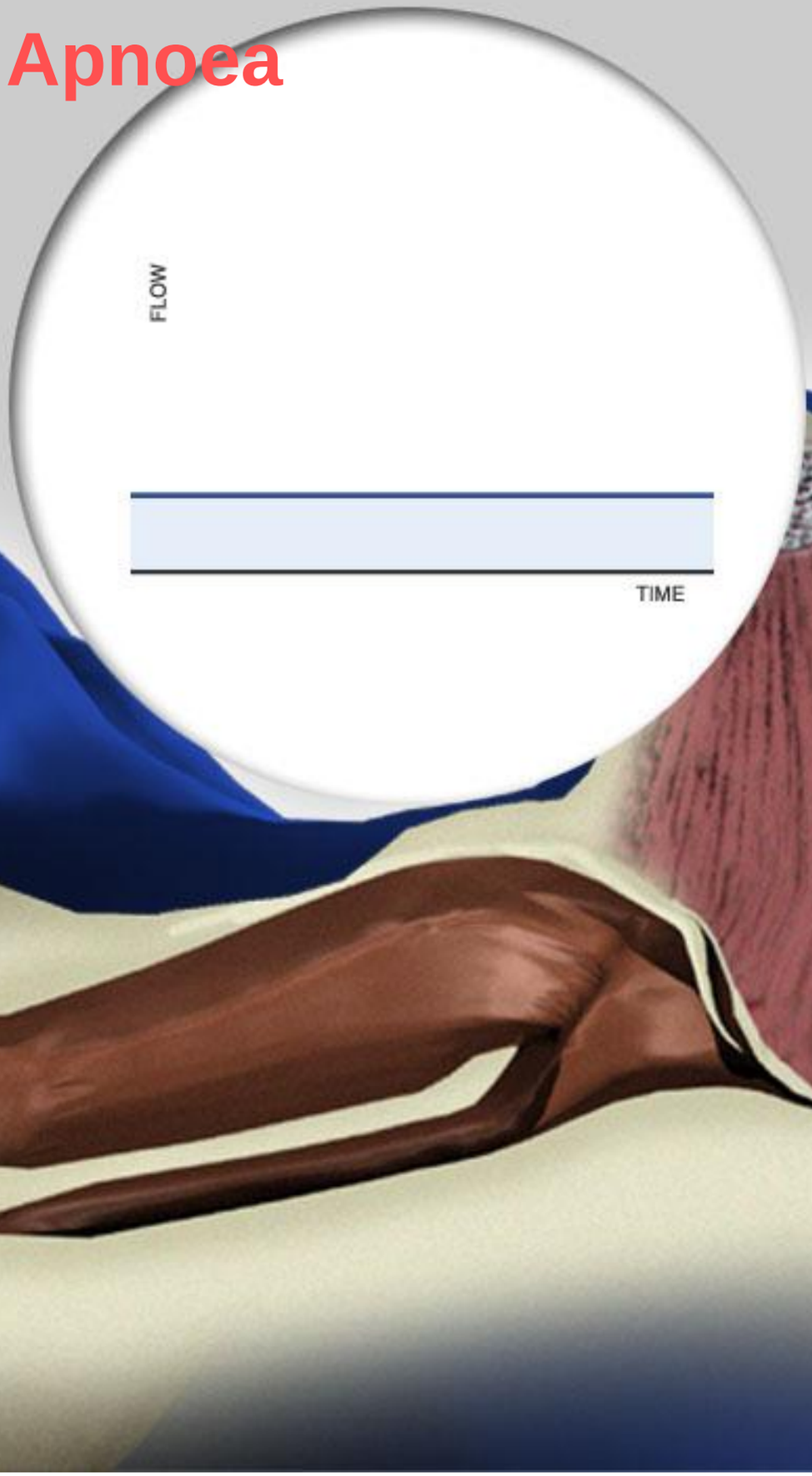
Flow Limitation



Snore



Apnoea



Sleep Jargon

- Apnoea
  - Cessation of breathing (< 80% of proceeding breath) for more than 10 seconds
- Obstructive
  - Due to pharyngeal collapse
- Central
  - Due to cessation of breathing effort
- Hypopnea
  - Reduction of breathing by at least 50% for more than 10 seconds with an associated drop> 3% oxygen saturation or EEG arousal.

THESE ARE NOW POOLED TOGETHER UNDER THE TERM SLEEP DISORDERED BREATHING (SDB)

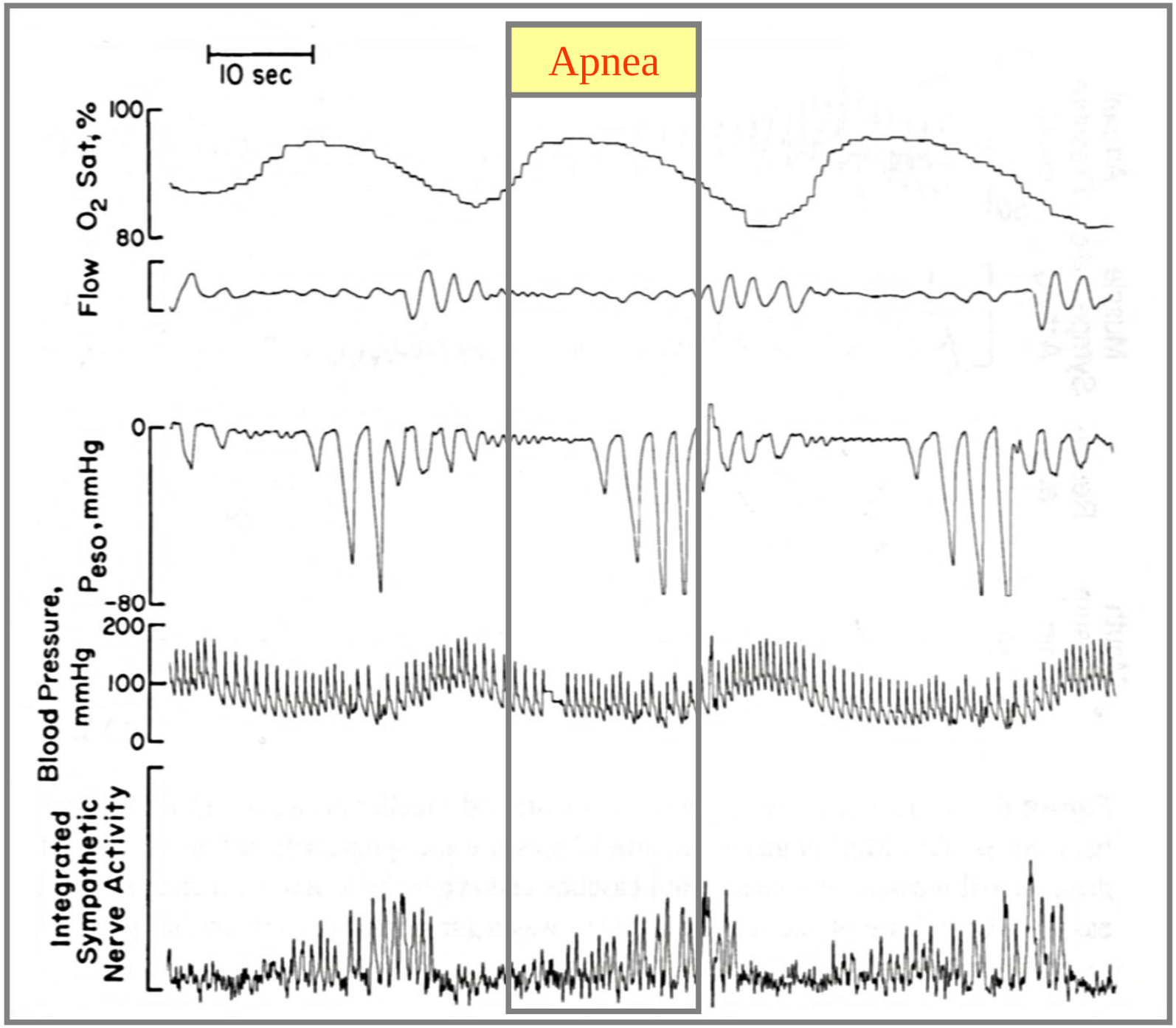
Physiological consequences of sleep apnea

Plunging blood oxygen saturation

Negative swings in intra-thoracic pressure

Increase in blood pressure

Surge in sympathetic nerve activity



Morgan *et al*., 1996 *Sleep*

Effects of OSA/SDB

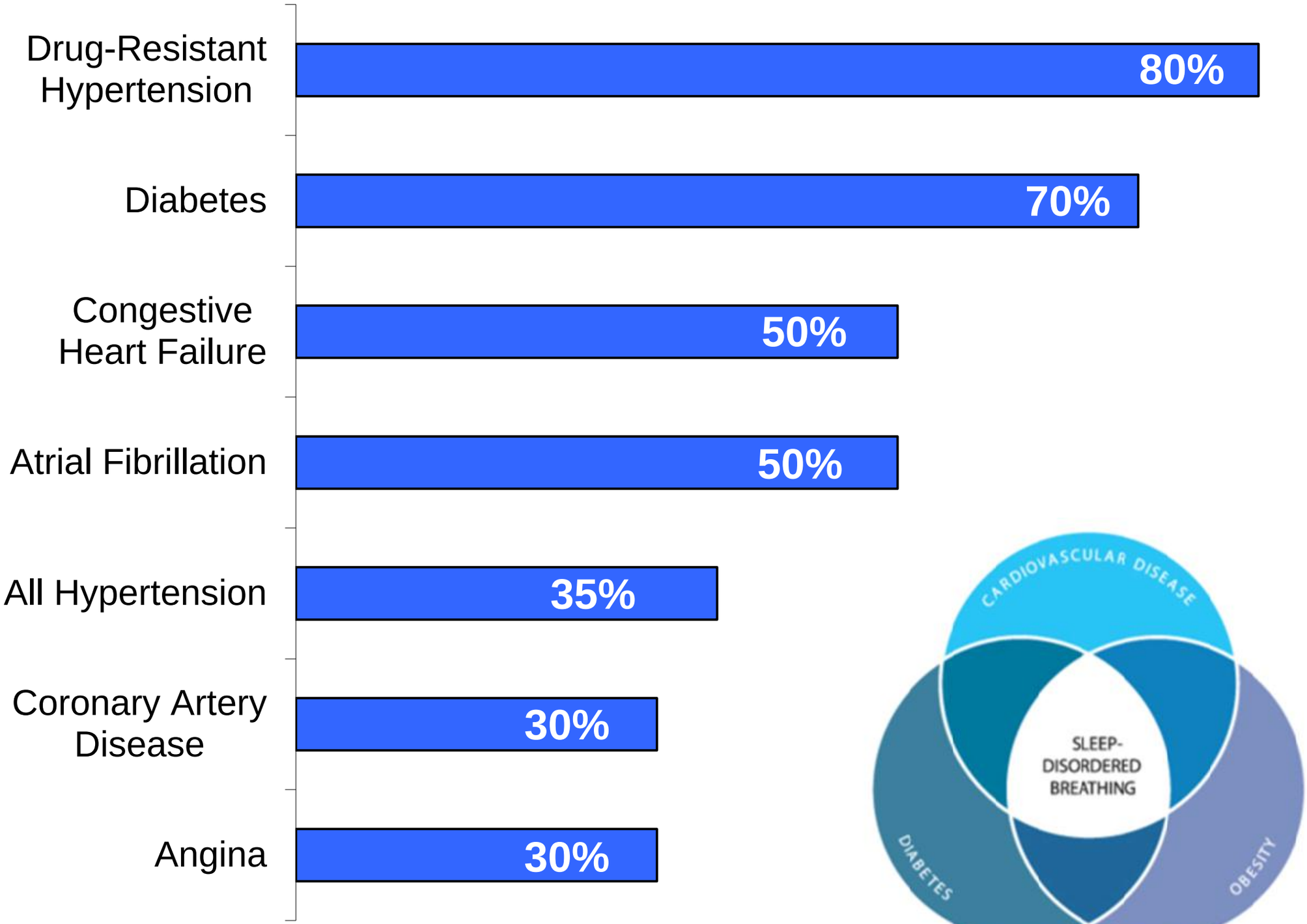
- OSA severity is typically defined by a measure of breathing (AHI), but this is only loosely related to either symptoms or long term consequences.

- Only patients exhibiting defined symptoms and levels of sleepiness are referred to overwhelmed sleep services.

- Epidemiological studies suggest that only a third to a quarter of patients with the breathing disorder have symptoms.

The important consequences are CARDIOVASCULAR

Sleep apnea prevalence



Logan et al.
J. Hypertension 2001

Einhorn et al.
Endocrine Prac 2007

Javaheri et al.
Circulation 1999

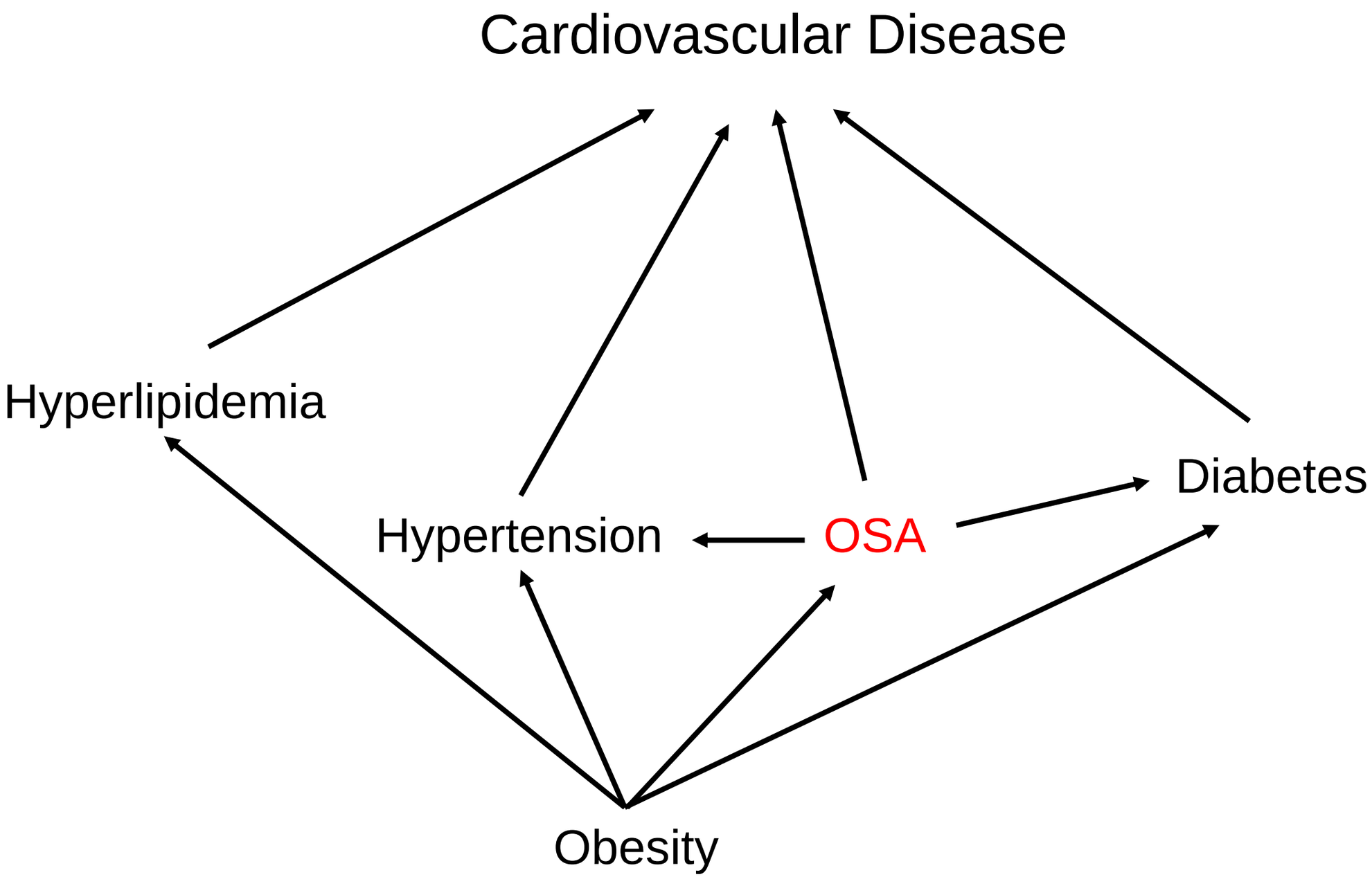
Somers et al.
Circulation 2004

Sjostrom et al.
Thorax 2002

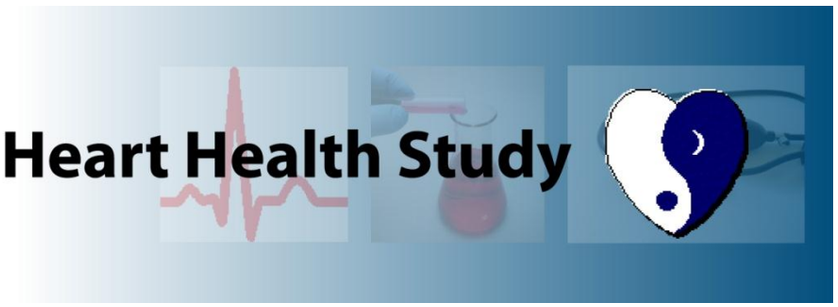
Schafer et al.
Cardiology 1999

Sanner et al.
Clin Cardiology 2001

Risk factors for co-morbidities



SDB and mortality

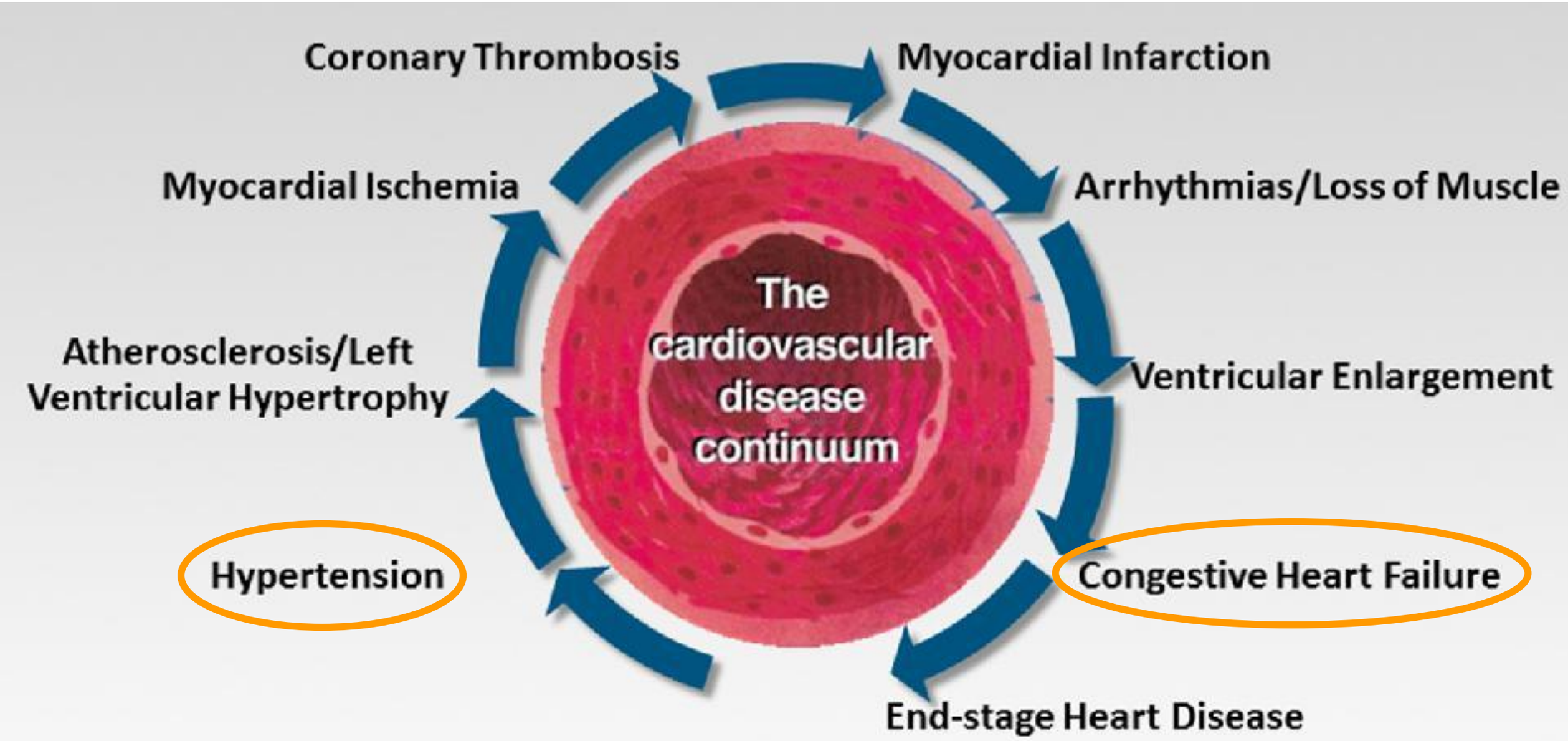


- 6,294 participants
- Average follow up period = 8.2 years
- **1.46 X more likely TO DIE with severe SDB**
- Predictor of mortality – nocturnal hypoxaemia

Punjabi *et al*., 2009 *PLoS Medicine*

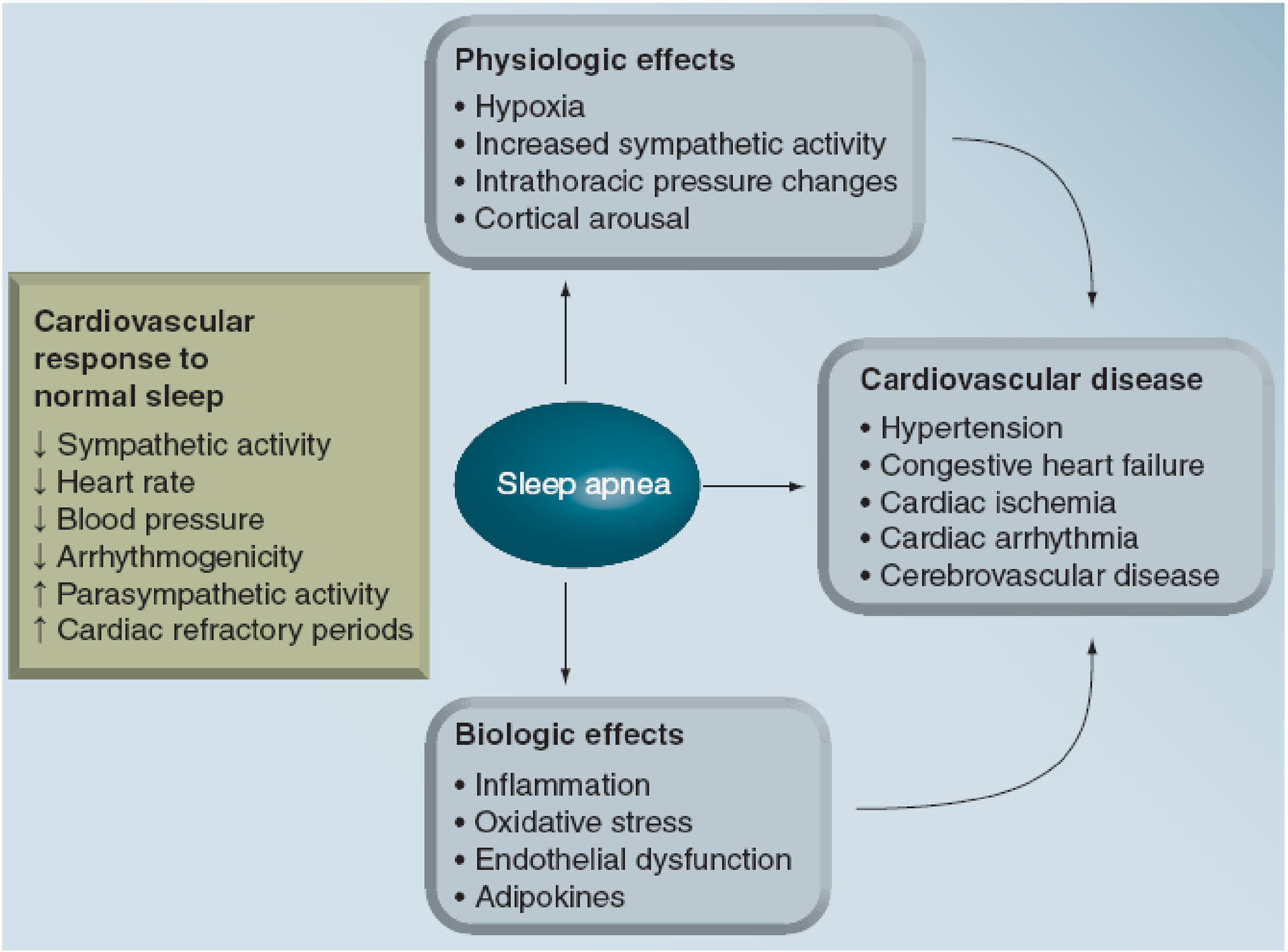
CARDIOVASCULAR

Cardiovascular disease continuum



Adapted from Dzau *et al*, 2006 *Circulation*

Sleep apnea – cardiovascular disease



Jean-Louis *et al*., 2010 *Expert Rev. Cardiovasc. Ther.*

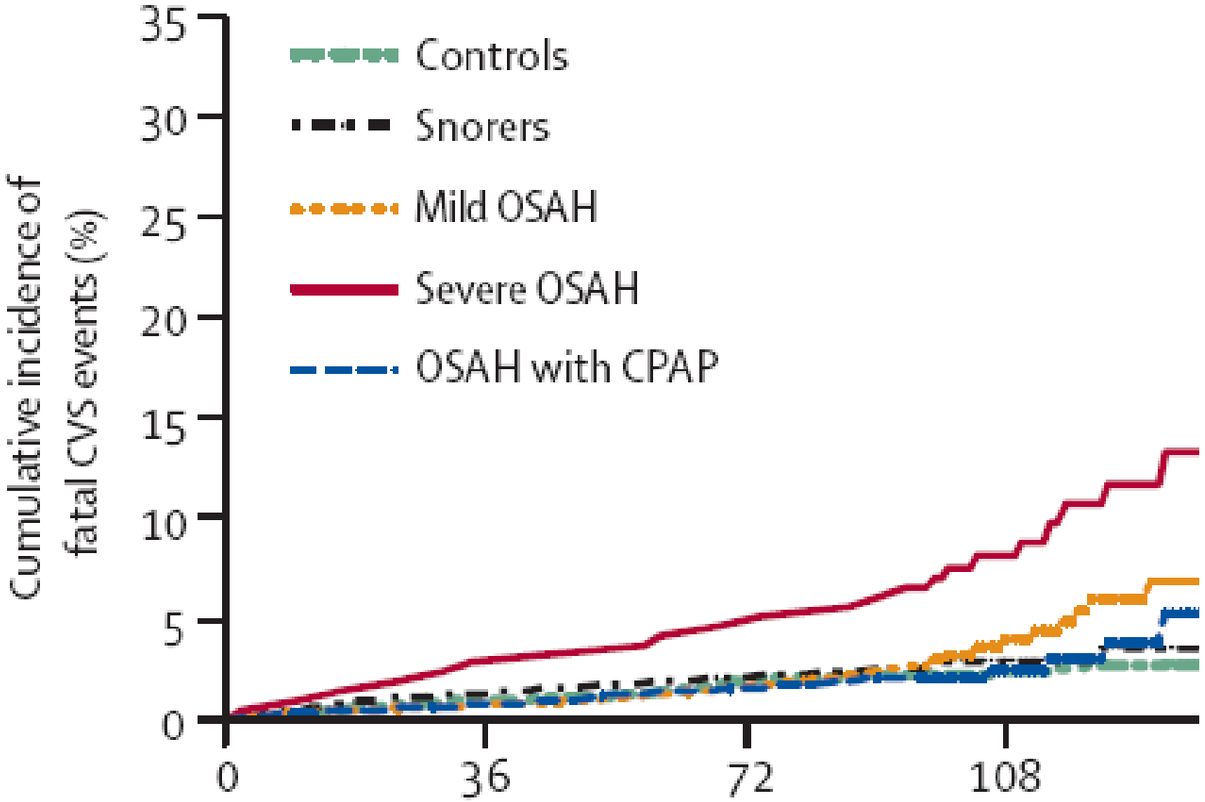
Wisconsin sleep cohort – 18 year follow up

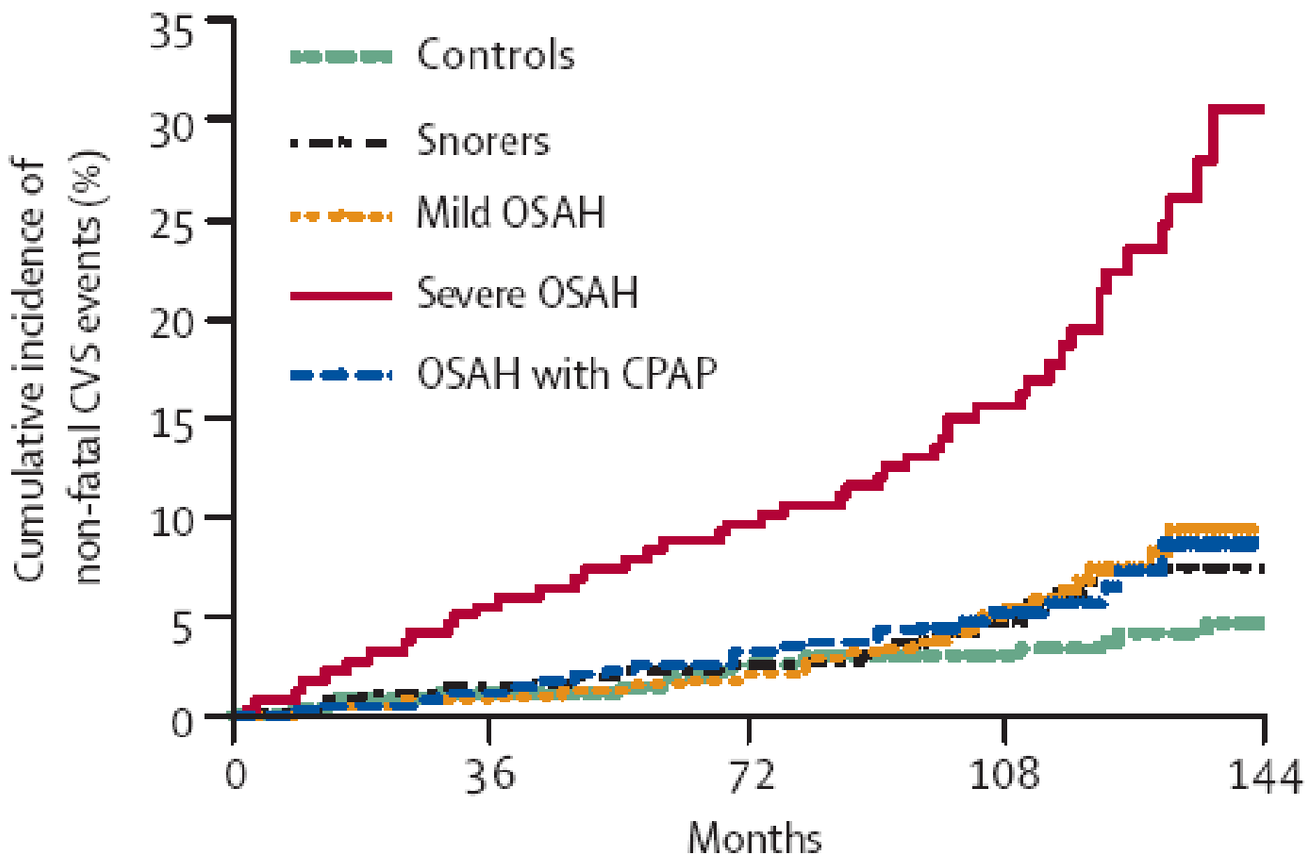
Baseline AHI category	Cardiovascular mortality Hazard Ratio (95% CI)
None: 0 - < 5	Reference
Mild: 5 - < 15	1.3 (0.4, 4.1)
Moderate: 15 - < 30	1.5 (0.3, 7.3)
Severe: ≥30	5.2 (1.4, 19.2)
	P-trend = 0.03

n = 1396

Young *et al.*, 2008 *SLEEP*

Long term fatal and non-fatal CVS events

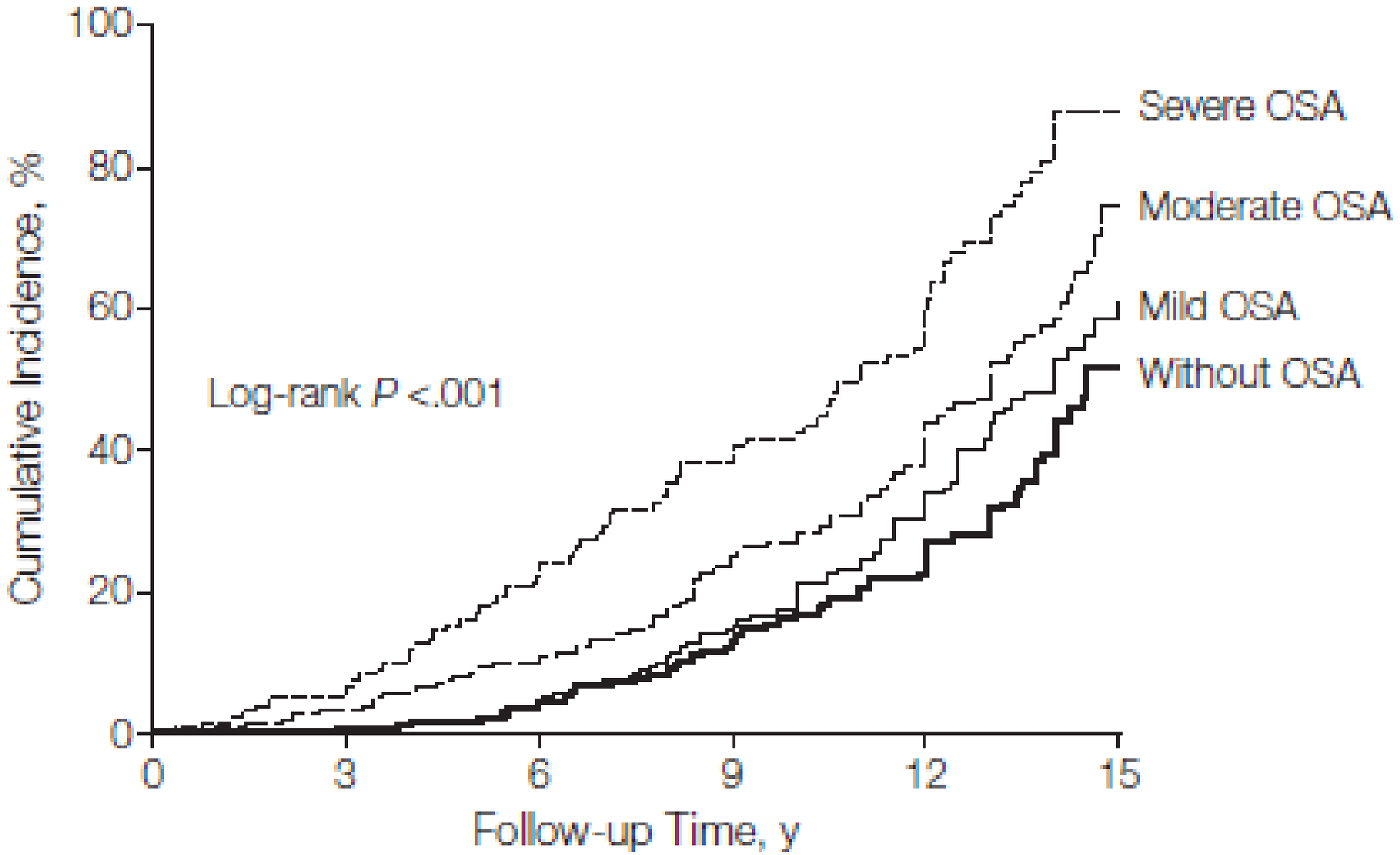




- 200-400 subjects per group
- Followed for a mean of 10.1 years

Marin *et al*., 2005 *Lancet*

Cumulative incidence of HT



n = 1889

Marin *et al.*, 2012 *JAMA*

RESISTANT HYPERTENSION

- Hypertension continuing despite 3 or more anti-hypertensive drugs

- Sleep study of 41 patients taking an average of 3.6 drugs.

- Average BMI of 34.

- 96% of men and 65% of women had OSA.

Logan et al Journal of Hypertension Dec 2001

EFFECT OF CPAP TREATMENT ON BLOOD PRESSURE IN PATIENTS WITH SDB

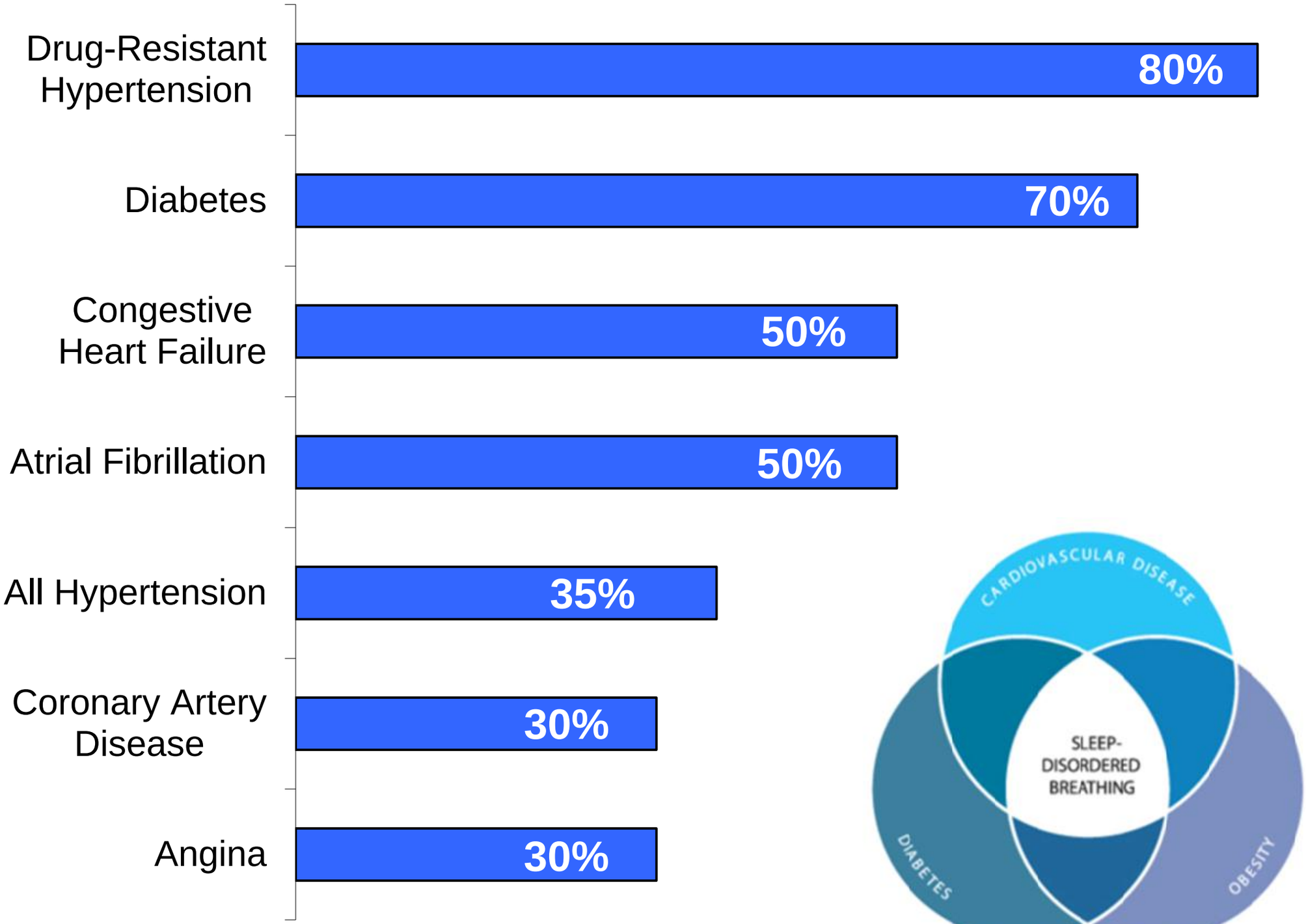
- 60 pts with moderate to severe OSA/SDB were randomized to effective or sub therapeutic nCPAP for 9 wks.
- PSM and continuous BP recordings (~ 19 hrs) were performed before and after CPAP Rx.
- 32 pts completed the study. AHI was decreased by ~ 95 and 50% in the effective and sub therapeutic Rx pts.
- Mean arterial BP decreased by 9.9+/-1.4 mmHg with effective Rx
- Mean, diastolic and systolic BP all decreased significantly by ~ 10 mmHg at night and during day.

Becker HF et.al. Circulation 2003;107:68-73.

SUMMARY
HYPERTENSION AND SDB

- There is unequivocal evidence of an association between hypertension and OSA/SDB independent of confounding factors.
- There is strong evidence that OSA/SDB is a cause of hypertension.
- OSA/SDB is prevalent in hypertension and very prevalent in drug resistant hypertension.
- Treatment of OSA/SDB with CPAP helps reduces blood pressure.

Sleep apnoea prevalence



Logan et al.
J. Hypertension 2001

Einhorn et al.
Endocrine Prac 2007

Javaheri et al.
Circulation 1999

Somers et al.
Circulation 2004

Sjostrom et al.
Thorax 2002

Schafer et al.
Cardiology 1999

Sanner et al.
Clin Cardiology 2001

Heart failure and SDB

- OSA is present in approximately a third of patients with HF
- CSA is present in approximately a third of patients with HF
- These effects are greater on a diseased LV than on normals

SDB may cause CHF, hastens it's progression and reduces survival

Recent Research

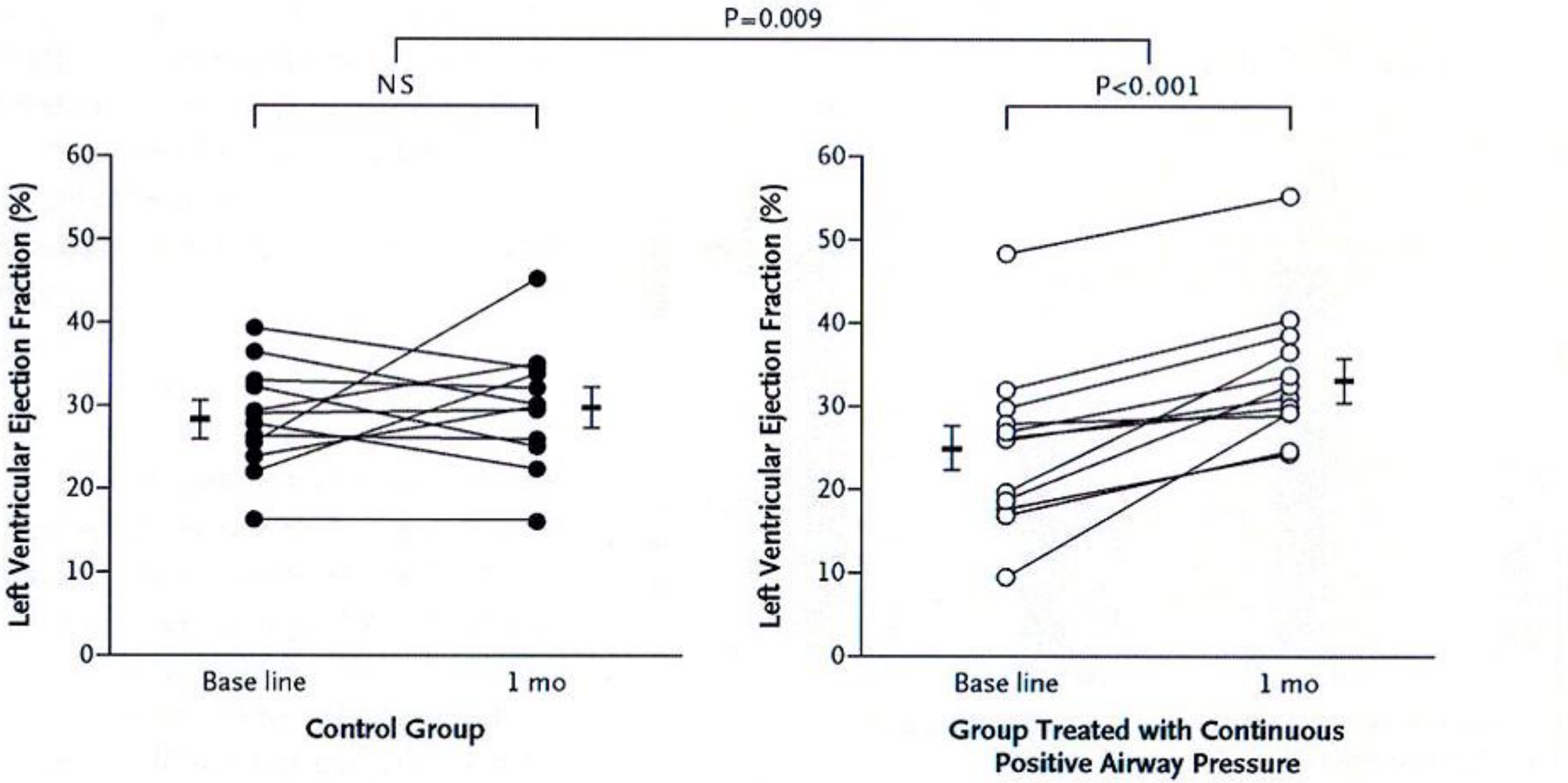
- Of the group that suffered heart attacks between midnight and 6am, **91% had undiagnosed OSA**.

- Of all the patients that had heart attacks, 70% of patients had undiagnosed OSA.

- The findings suggest that OSA might be a trigger for heart attacks
-
- The influence of OSA on the timing of these patients heart attacks could not be explained by comorbidities or medication differences.

Virend Somers et al ***American College of Cardiology 2010***

Heart failure - effect of CPAP on LV function



Kaneko *et al*., 2003 *NEJM*

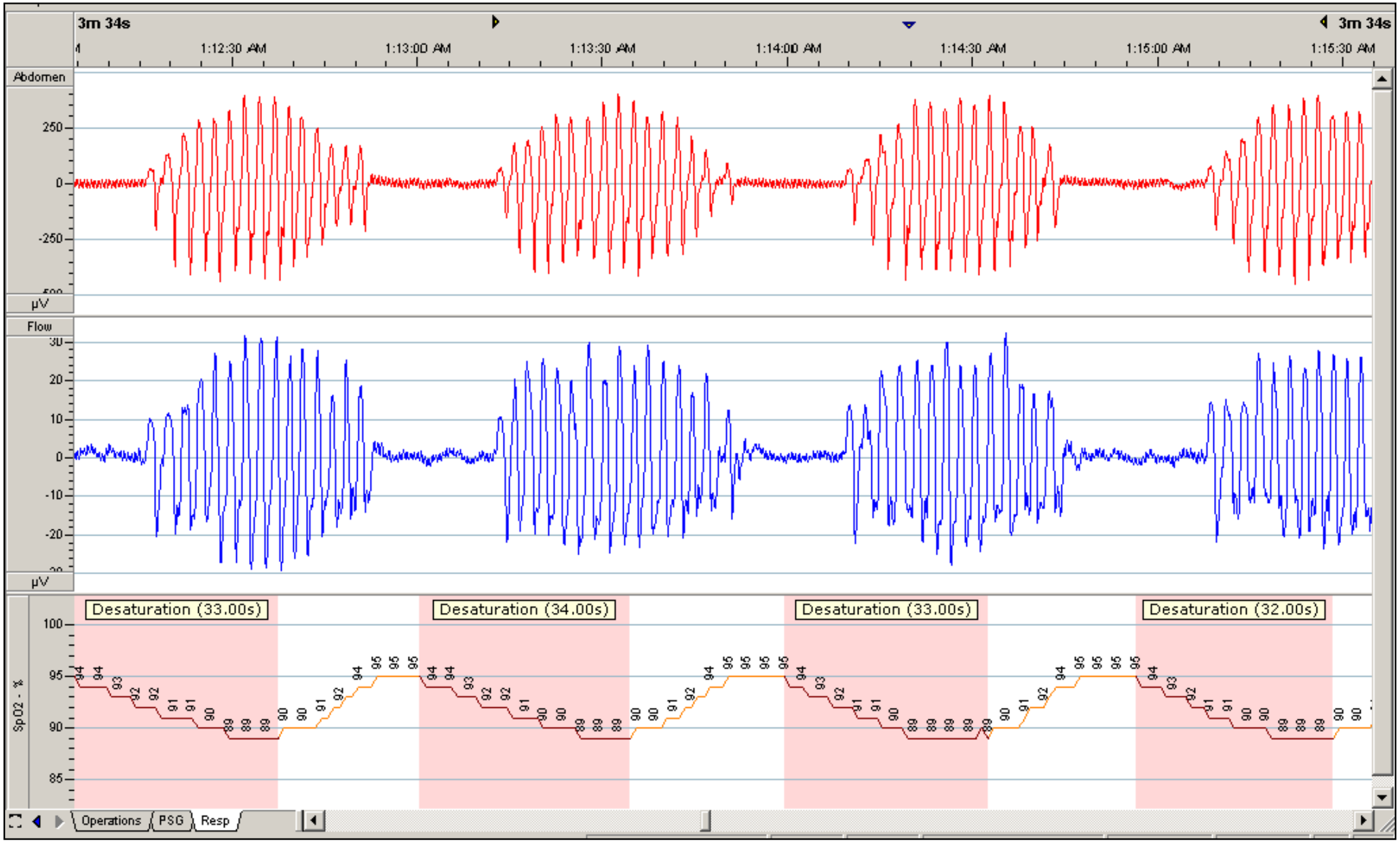
CPAP on LVEF

- 27 patients that were newly identified to have OSA (avg AHI 42±21).
- LVEF improved in 1 month and was sustained at 3 months with the addition of nCPAP

Seiji Koga, Satoshi Ikeda, Jungo Urata and Shigeru Kohno

The American Journal of Cardiology, Volume 101, Issue 12, 15 June 2008, Pages 1796-1800

Cheyne Stokes Respiration



CHF and CSA/CSR *Mechanism for the development of CSR*

- CSR secondary to CHF and related to severity of ventricular dysfunction
- Cause is not fully understood
- Contributing factors believed to be:
  - Wet lungs (pulmonary edema)
  - High PCWP (preload)
  - Increased circulatory times (delayed response to changing blood gas levels)
  - Chemoreceptor hypersensitivity to CO_2

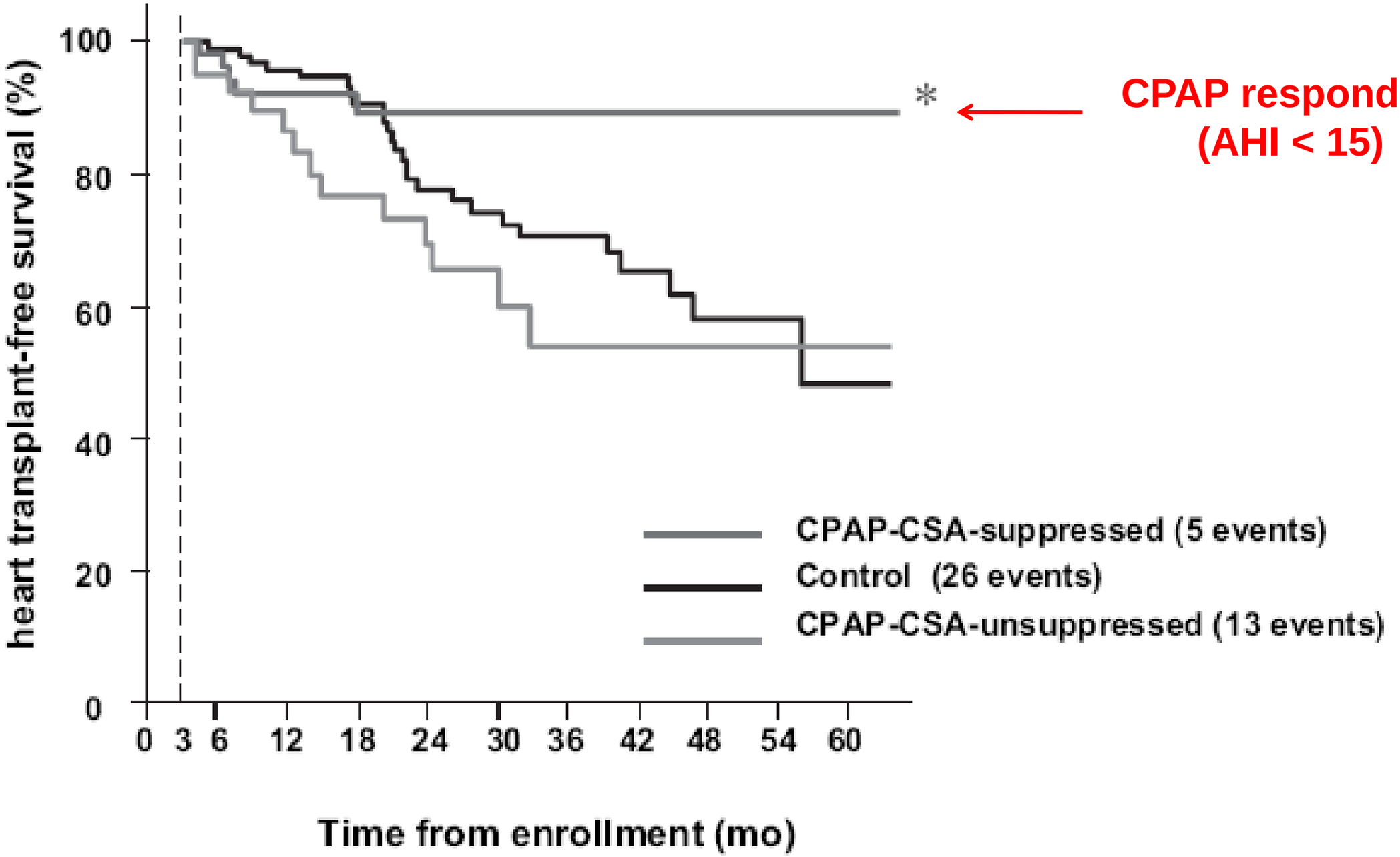
CHF and CSA/CSR Consequences

- CSR is believed to accelerate HF by causing:
  - Repetitive hypoxia
  - Increased SNS activity
  - Increased afterload
  - Oscillations in heart rate and blood pressure
- Results in independent adverse effects on survival:
  - Increased risk for death
  - Increased cardiac transplantation rate

- **CSR also results in fatigue and daytime hypersomnolence**

Lanfranchi et al. *Circulation* 1999; Sin et al. *Circulation* 2000; Hanly & Zuberi-Khokhar. *Am J Respir Crit Care Med* 1996

HF – suppressed vs unsuppressed CSA with CPAP



CANPAP Post Hoc Analysis

Artz *et al*., 2007 *Circulation*

TAKE HOME MESSAGE

Sleep disordered breathing increases mortality

- **CARDIOVASCULAR**
  - SDB is very common and affects prognosis
  - Cardiovascular diseases are probably the most important consequence of OSA
  - Assessment of SDB is rapidly becoming a routine part of the management of hypertensive/cardiology patients
  - **At home Cardio Respiratory Sleep Studies have simplified the pathway to treatment for at risk groups**

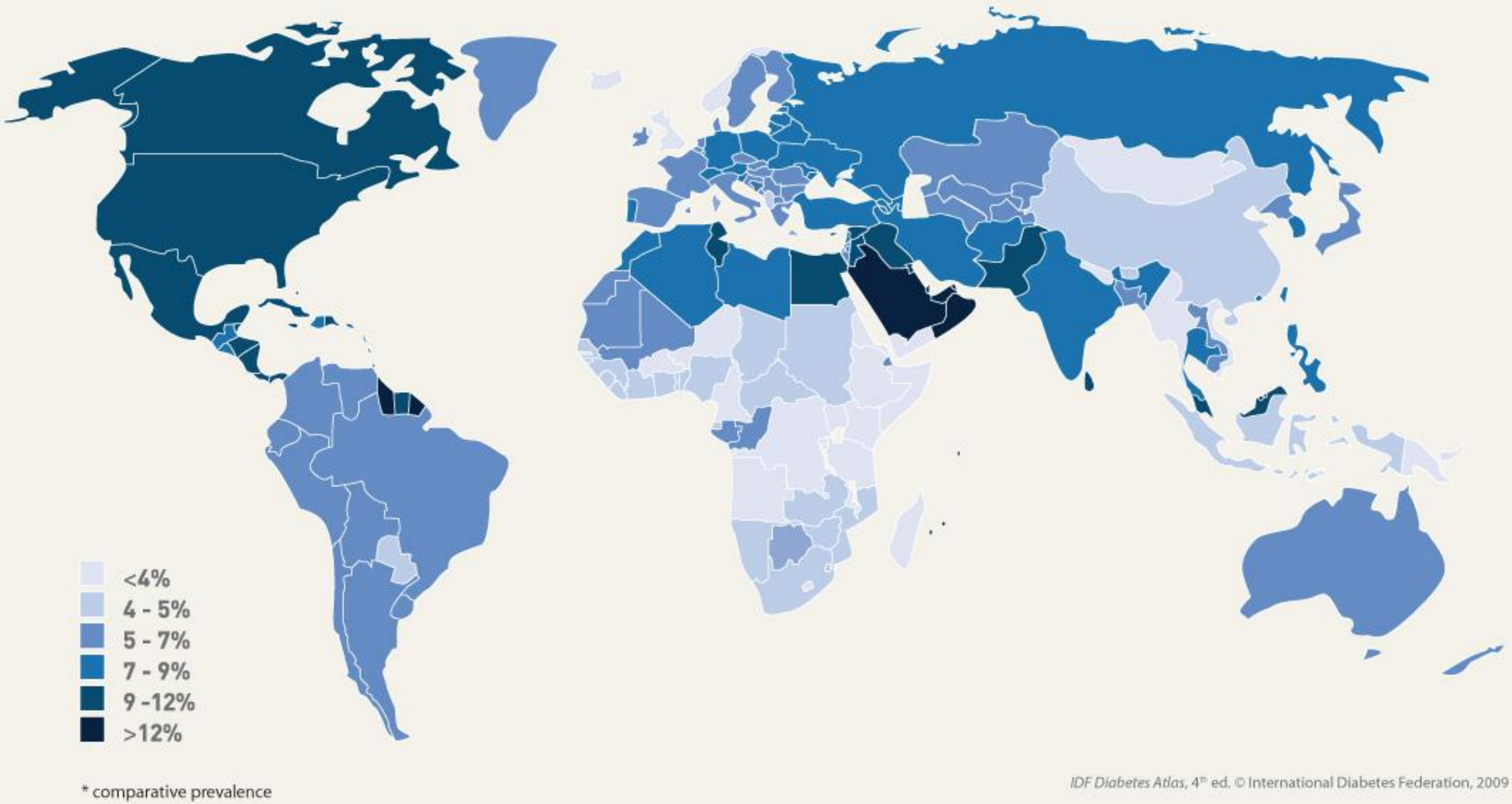
And Finally…….

ANY QUESTIONS?

DIABETES

Diabetes prevalence: 2010

MAP 2.1 Prevalence* (%) estimates of diabetes (20-79 years), 2010

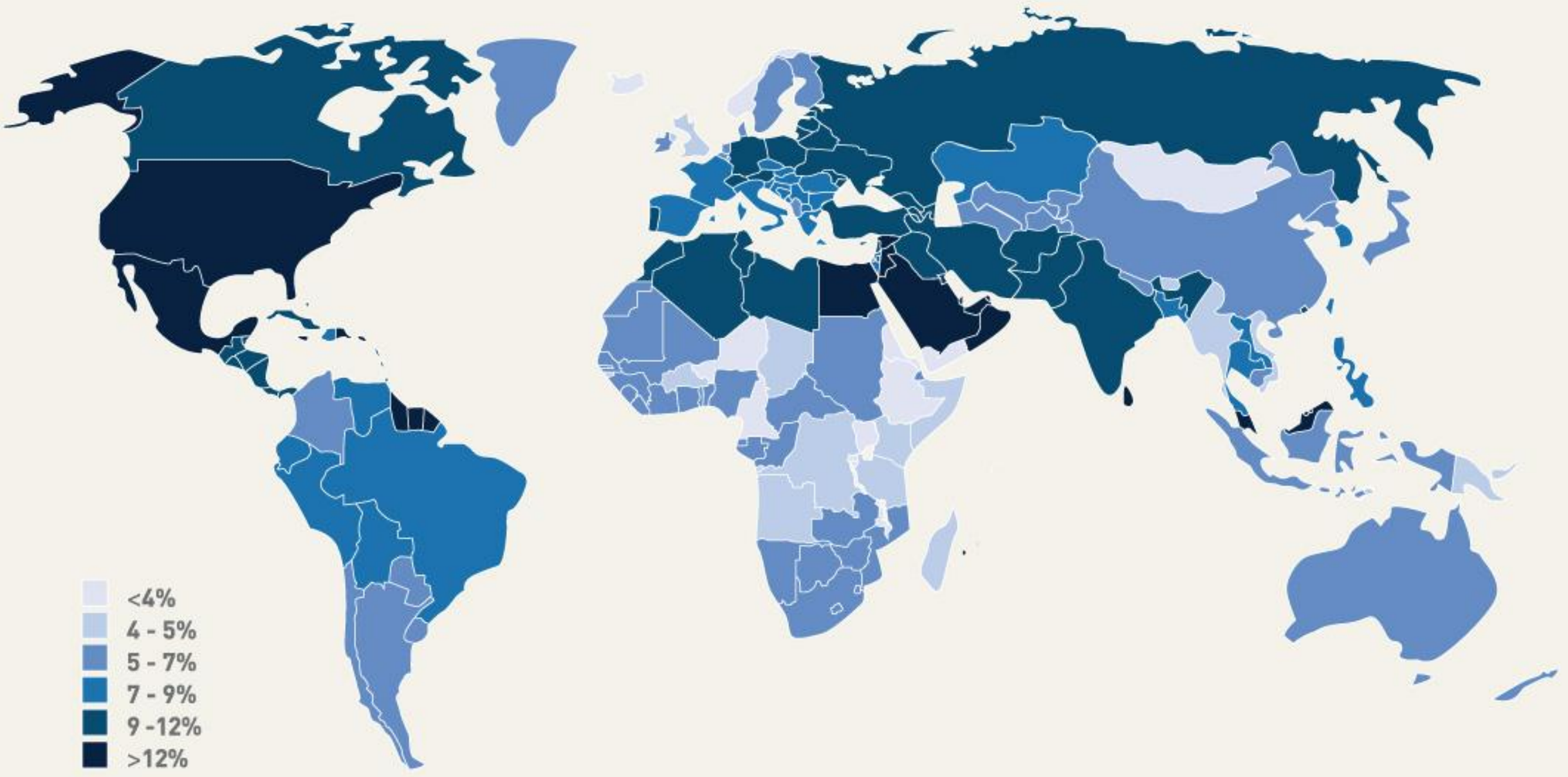


* comparative prevalence

IDF Diabetes Atlas, 4th ed. © International Diabetes Federation, 2009

Diabetes prevalence: 2030

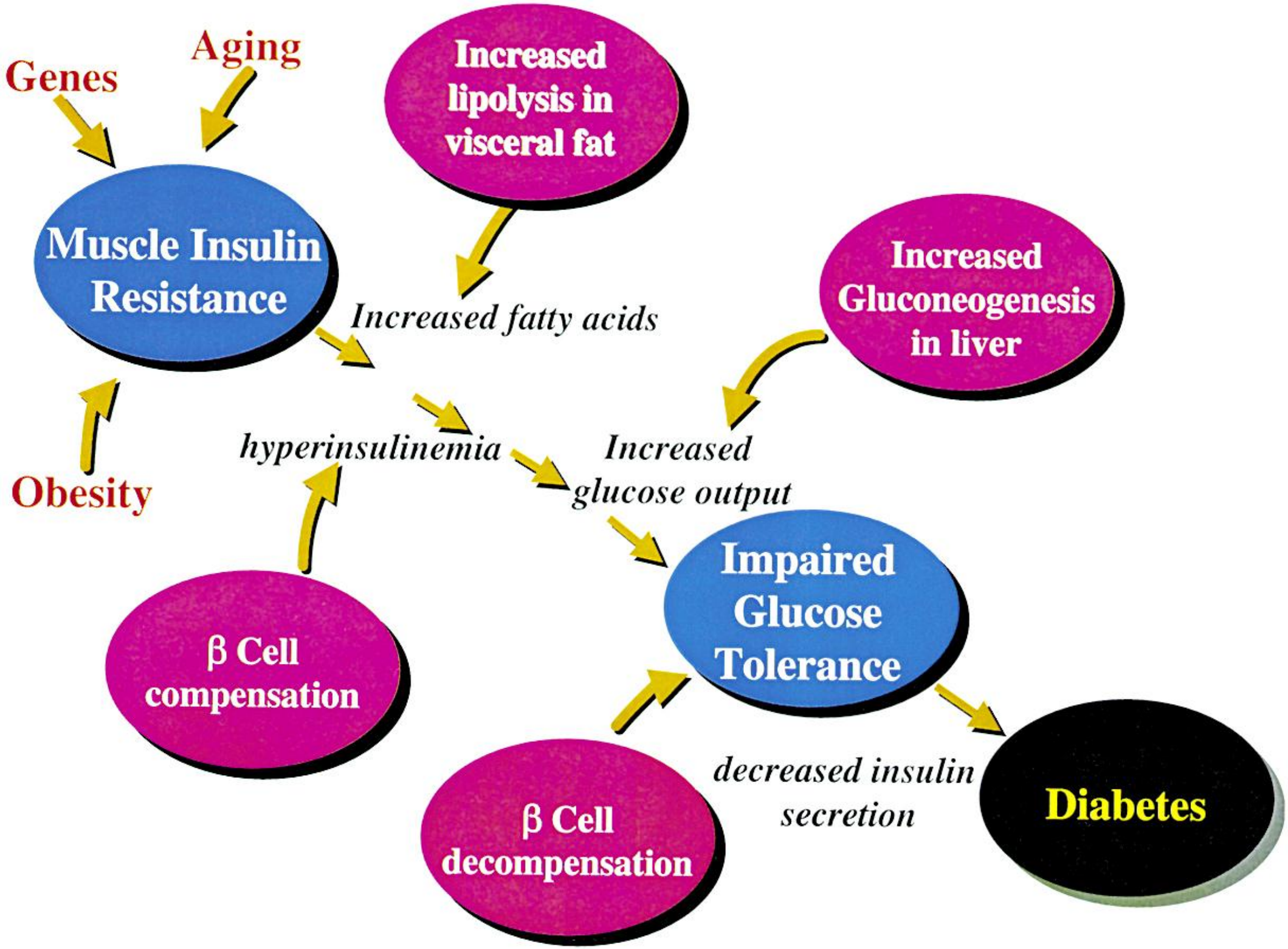
MAP 2.2 Prevalence* (%) estimates of diabetes (20-79 years), 2030



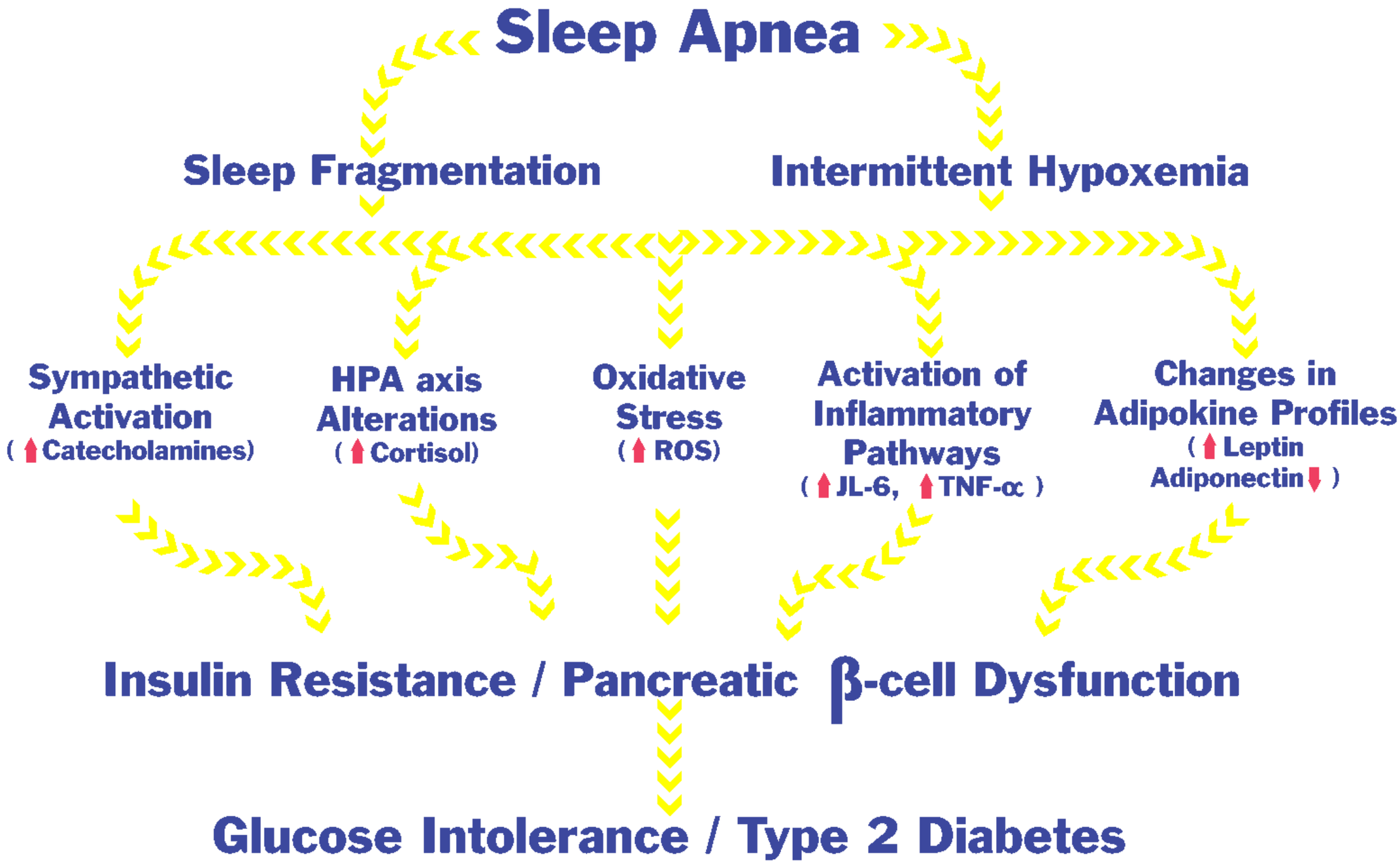
* comparative prevalence

IDF Diabetes Atlas, 4th ed. © International Diabetes Federation, 2009

Insulin resistance is the first step



Potential mechanisms



Adapted from Punjabi *et al*, 2005 *J Appl Physiol*

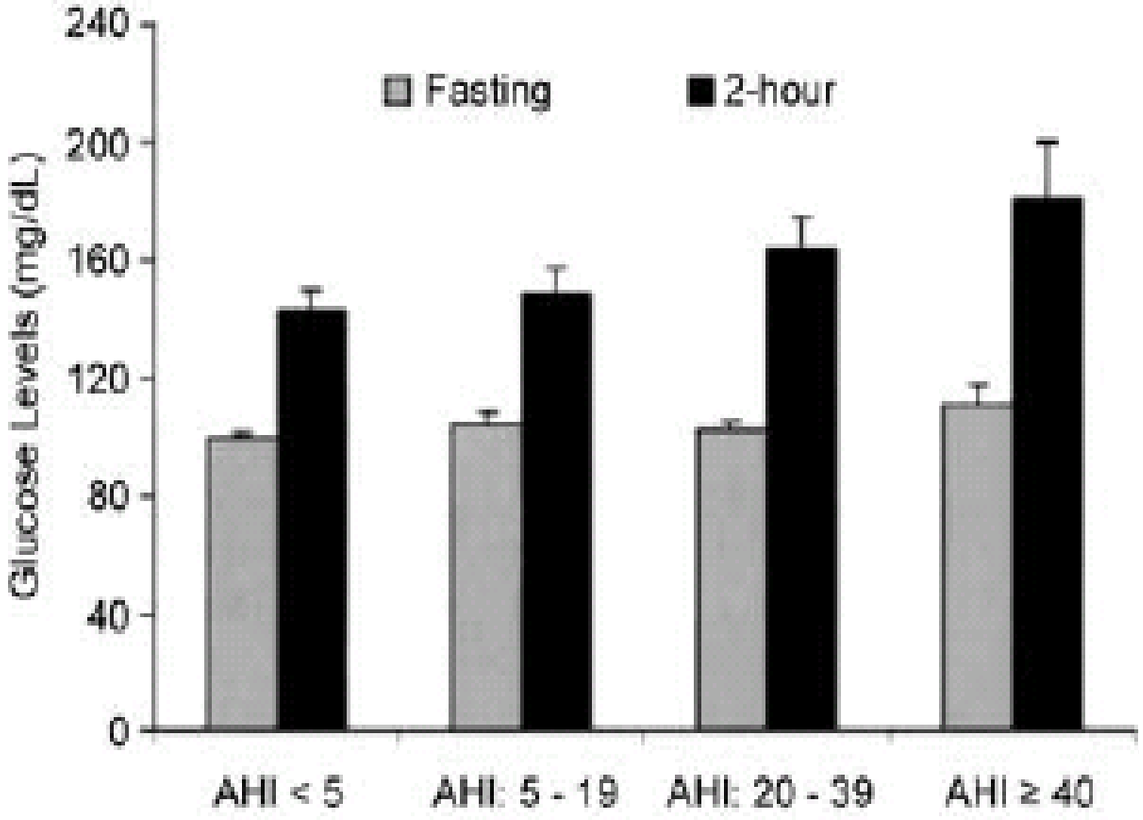
OSA and T2DM: Wisconsin sleep cohort study

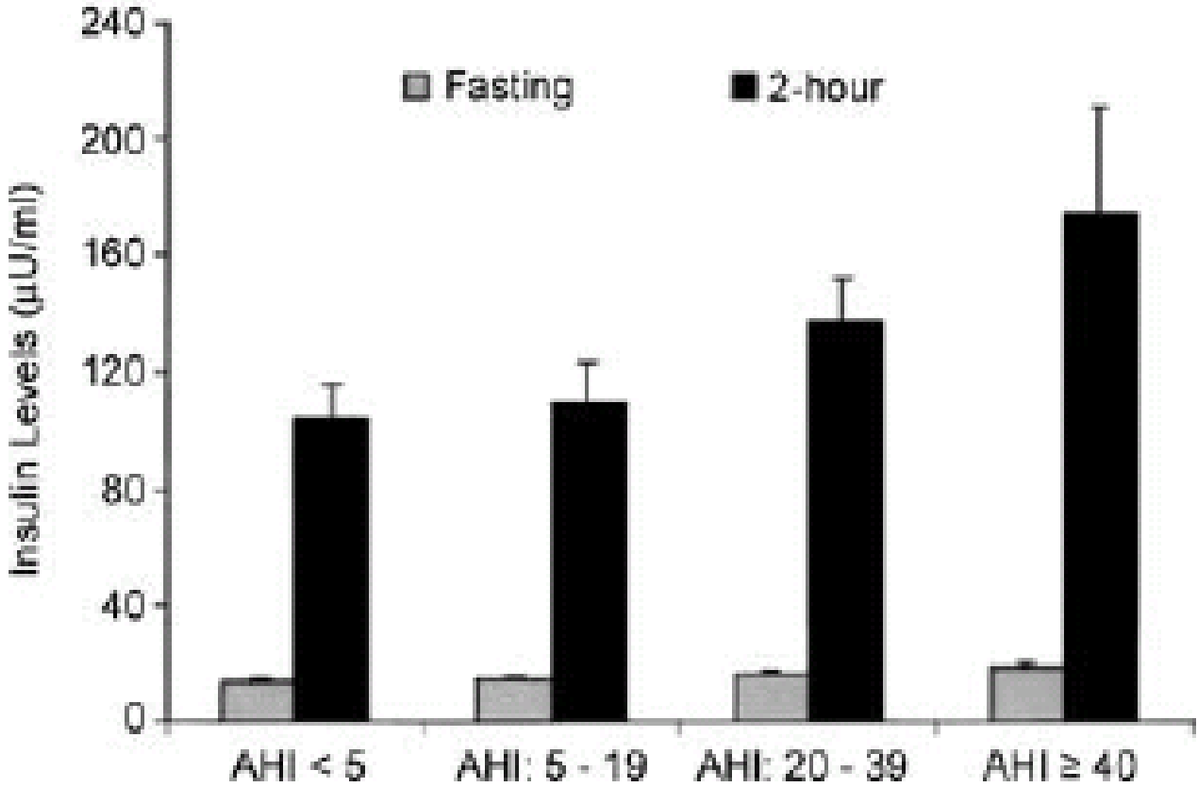
Odd Ratios for Incident Type 2 Diabetes

	Odds Ratio	95% Confidence Interval	*p-v*alue
Adjusted for sex and age			
AHI 5 – 15 vs AHI < 5	2.81	1.51 – 5.23	0.001
AHI ≥ 15 vs AHI < 5	4.06	1.86 – 8.85	0.0004
Adjusted for sex, age, and body habitus measures*			
AHI 5 – 15 vs AHI < 5	1.56	0.80 – 3.02	0.19
AHI ≥ 15 vs AHI < 5	1.62	0.67 – 3.65	0.24

Reichmuth *et al*., 2005 *Am J Respir Crit Care Med*

Glucose intolerance and insulin resistance to AHI

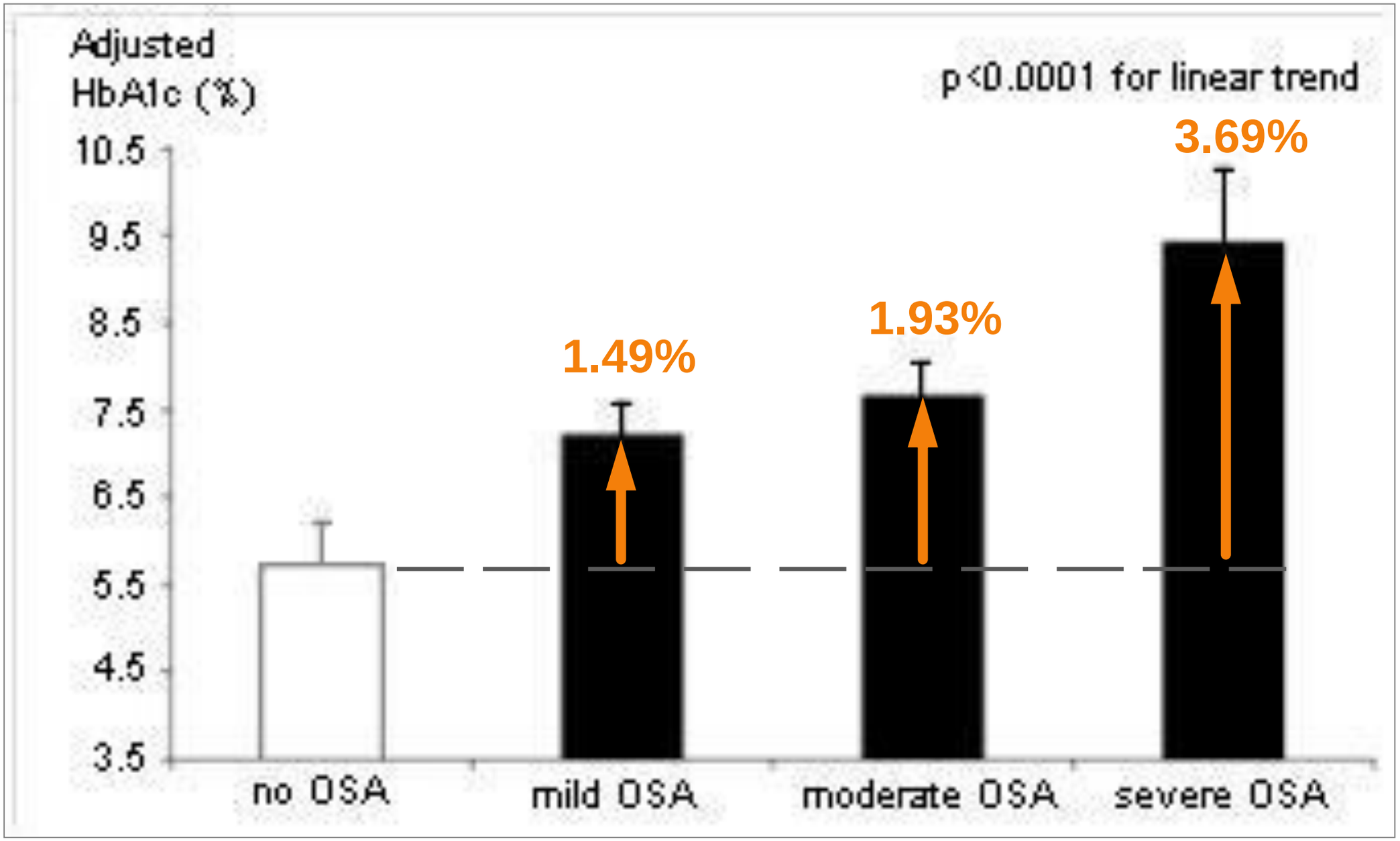




- Healthy population (no diabetes or cardiovascular disease)
- n=150

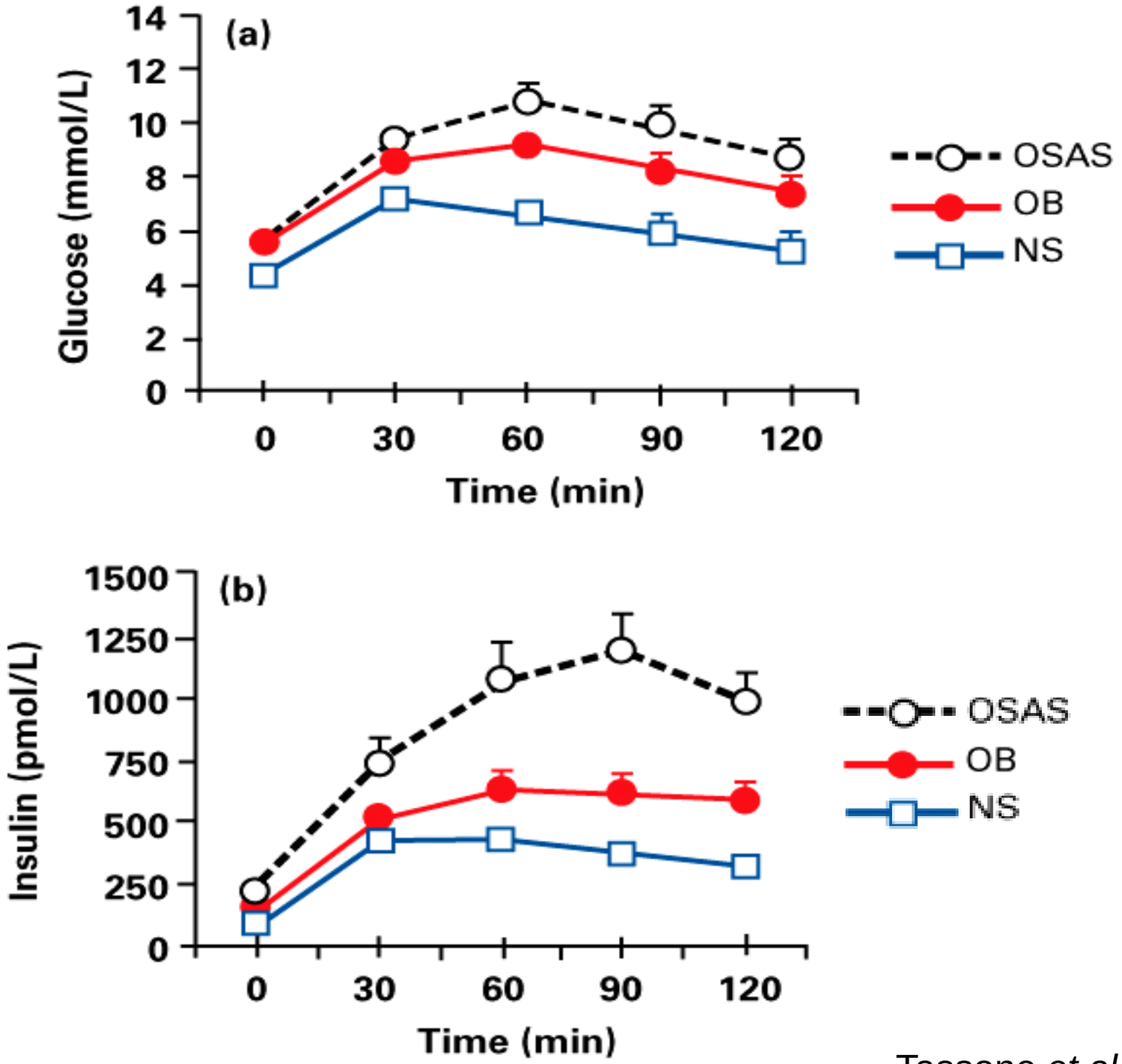
Punjabi *et al.*, 2002 *AJRCCM*

OSA Severity and Blood Glucose Levels



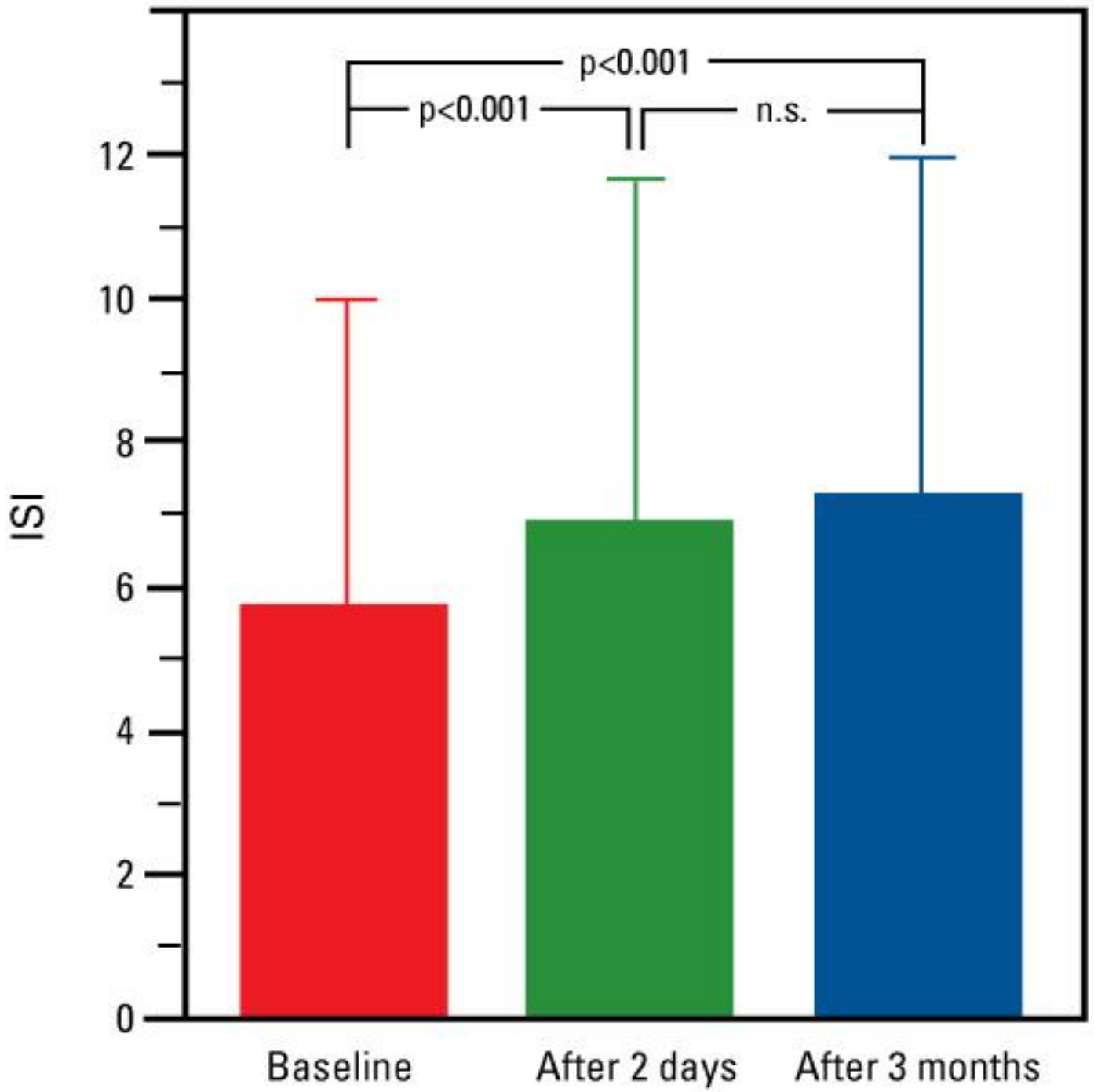
Aronsohn *et al,* 2010 *AJRCCM*

Insulin resistance – obesity independent



Tassone *et al.*, 2003 *Clin Endocrinol*

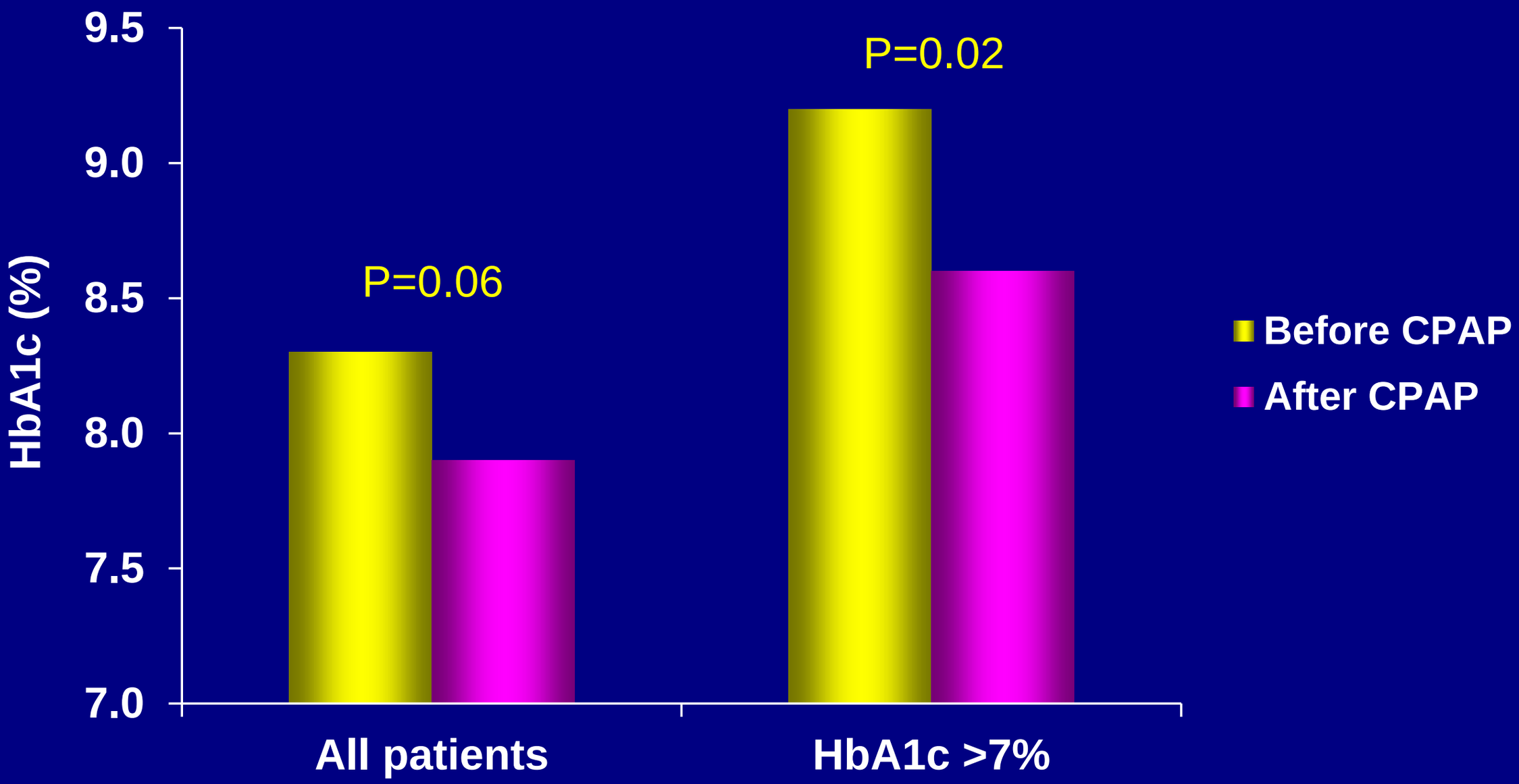
CPAP improves insulin sensitivity



Improvement of insulin sensitivity index (ISI) after onset CPAP treatment in 31 patients

Harsh *et al,* 2004 *AJRCCM*

HbA1c before and after 3 months of CPAP



Babu *et al*. 2005 *Arch Intern Med*

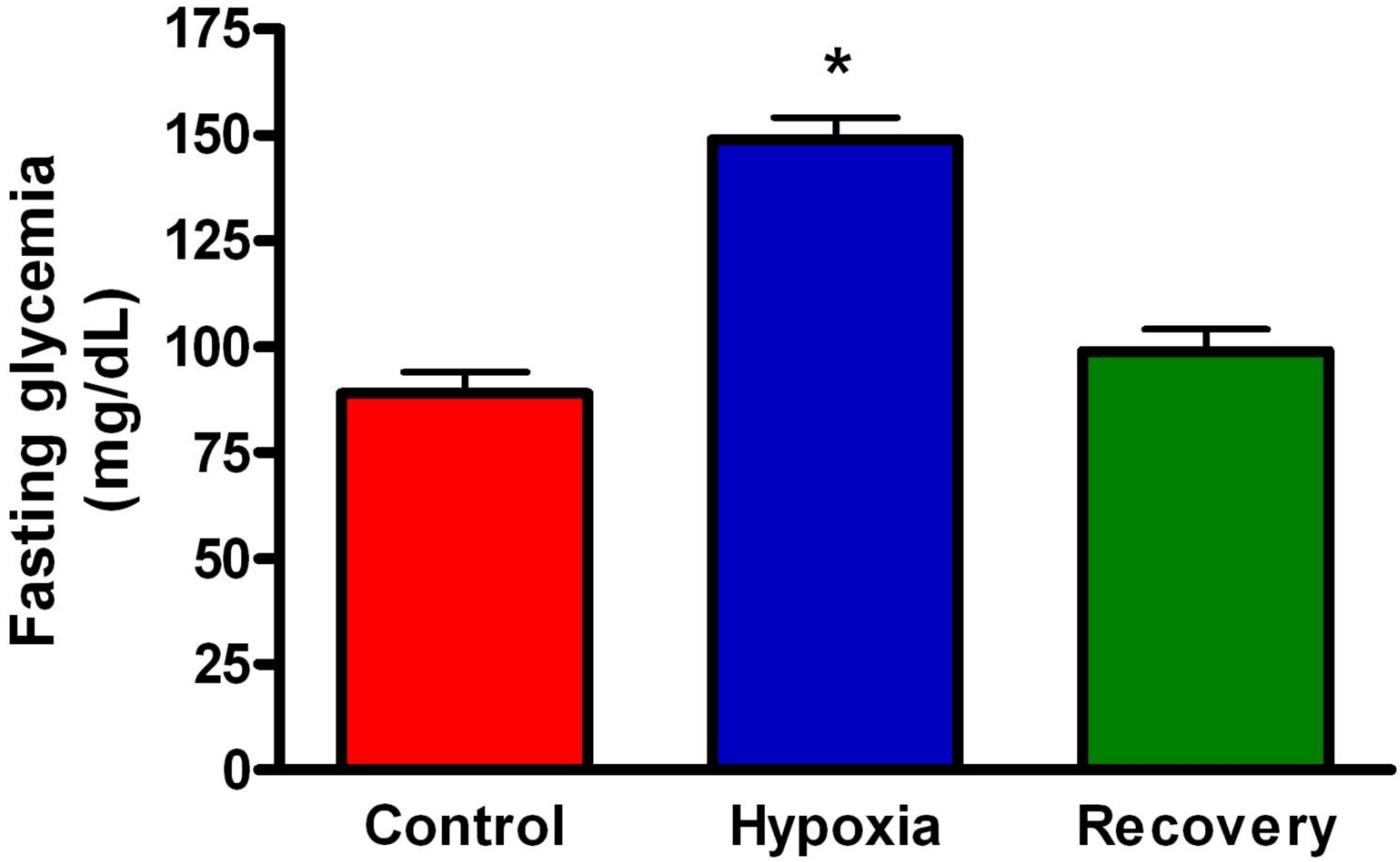
CPAP and metabolic syndrome

Table 3. Effects of CPAP versus Sham CPAP on Components of the Metabolic Syndrome.*

Variable	Treatment Effect		Difference or Odds Ratio (95% CI)	P Value†
	CPAP (N=86)	Sham CPAP (N=86)		
Abdominal circumference — cm	−0.53±2.42	0.20±3.49	−0.73 (−2.15 to 0.68)	0.32
Systolic blood pressure — mm Hg	−3.07±8.02	0.79±7.22	−3.86 (−6.37 to −1.35)	0.001
Diastolic blood pressure — mm Hg	−2.81±6.07	−0.33±5.25	−2.49 (−4.13 to −0.85)	<0.001
Fasting blood glucose — mg/dl	−1.78±11.37	−0.43±9.40	−1.35 (−4.43 to 1.74)	0.10
Fasting insulin — mU/liter	1.75±11.48	3.33±14.54	−1.59 (−5.60 to 2.42)	0.35
Insulin resistance	0.42±3.10	0.81±3.67	−0.39 (−1.40 to 0.62)	0.23
Glycated hemoglobin — %	−0.03±0.42	0.19±0.49	−0.21 (−0.36 to −0.07)	0.003
Triglycerides — mg/dl	−18.86±71.43	−0.21±80.75	−18.65 (−41.57 to 4.27)	0.02
Cholesterol — mg/dl				
Total	−9.36±31.46	3.90±21.95	−13.26 (−21.25 to −5.28)	0.005
HDL	−0.05±12.85	−0.08±12.28	0.04 (−3.82 to 3.89)	0.75
LDL	−5.72±26.56	3.83±20.44	−9.55 (−16.65 to −2.46)	0.008
Non-HDL	−9.32±32.94	3.98±22.74	−13.30 (−21.79 to −4.82)	0.009
HDL:total cholesterol	0.01±0.07	−0.01±0.07	0.02 (−0.01 to 0.04)	0.01
LDL:total cholesterol	0.00±0.08	0.01±0.07	−0.01 (−0.03 to 0.01)	0.58
Reversal of the metabolic syndrome — no. (%)	11 (13)	1 (1)	12 (9 to 99)	0.003

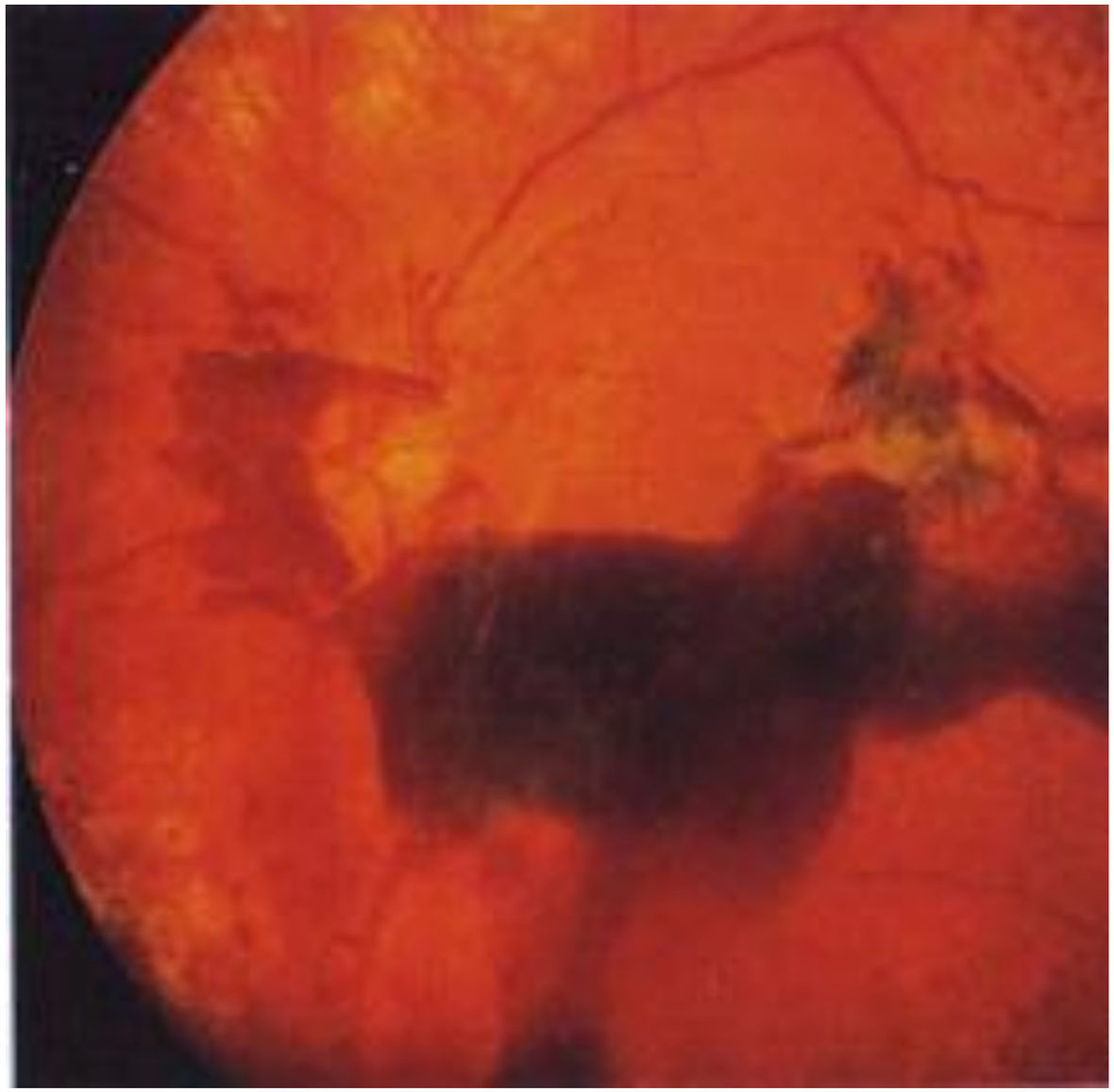
Sharma *et al.*, 2011 *NEJM*

Intermittent hypoxia: fasting glycaemia



Polak *et al.*, 2012 *AJRCCM* (submitted)

Diabetic retinopathy



West *et al*., 2010 *Diabetic Med.*

- Retinal cells are very susceptible to hypoxia
- OSA causes recurrent hypoxia
- High prevalence of OSA in diabetics with retinopathy
- Retinopathy significantly worse with OSA
- OSA independent significant predictor of retinopathy

IDF consensus statement (2008)

International Diabetes Federation

IDF recommendations to healthcare professionals

- Healthcare professionals working in both type 2 diabetes and OSA need to be aware, educated and trained about the link between both conditions. They should aim to develop routine interventions that are appropriate for both conditions.
- People with OSA should be routinely screened for possible metabolic disorders and cardiovascular risk.
- People with type 2 diabetes should be screened for OSA particularly when they present with classical symptoms such as witnessed apneas, heavy snoring or daytime sleepiness.

Conclusions

Sleep disordered breathing increases mortality

- **CARDIOVASCULAR**
  - SDB is very common and affects prognosis
  - Cardiovascular diseases are probably the most important consequence of OSA
  - Assessment of SDB is rapidly becoming a routine part of the management of cardiology patients

- **DIABETES**
  - OSA and type 2 diabetes frequently coexist
  - Accumulating evidence that OSA impairs glucose metabolism
  - Rapidly increasing awareness of OSA in the diabetes community and assessment/management should INCREASE